Synopsis for Registration as Research Student

for

Doctoral Degree

on

A Novel Approach for Brain Tumor Segmentation and Analysis

By

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1 Introduction

Among various diseases, cancer has become a big threat to human beings globally. The world's population is expected to be 7.5 billion by 2020 and approximations predict that about 15.0 million new cancer cases will be diagnosed; with deaths of about 12.0 million cancer patients. As per Indian population census data, Cancer is the second most common disease in India responsible for maximum mortality with about 0.6 million deaths per year [1].

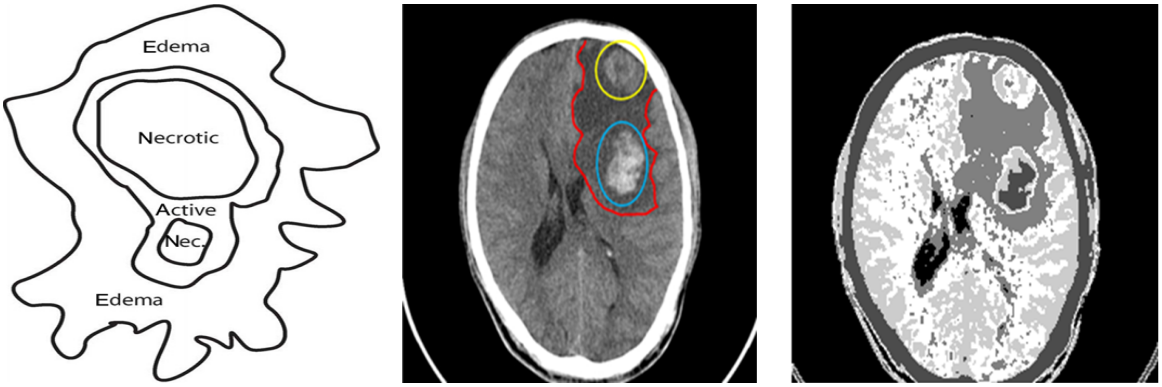
What is tumor?

The organs and tissues of the body are made up of tiny building blocks called cells. Cancer is a disease of these cells. Cells in different parts of the body may look and work differently but most reproduce themselves in the same way. Cells are constantly becoming old and dying, and new cells are produced to replace them. Normally, cells divide in an orderly and controlled manner. If for some reason the process gets out of control, the cells carry on dividing, developing into a lump which is called a tumor. When this abnormality is detected in brain it is termed as **Brain Tumor**. It is important to note that 20 % of all cancer spreads to brain.

According to the study of World Health Organization (WHO) there are more than 100 types of brain tumors. Generally most of the brain tumors have edema, necrotic cells and active cells as shown in Figure 1. From diagnostic perspective it is very important to segment these sub parts of tumor. Because of non-homogeneous intensity distribution, background noise, complex shape, unclear boundries and low intensity contrast between adjacent brain tissues segmentation becomes a challenging task.

Depending upon the severity Brain Tumors are Graded into four categories as:

- Grade I : The tissue is benign. The cells look nearly like normal brain cells, and they grow slowly.
- Grade II : The tissue is malignant. The cells look less like normal cells than the cells in a Grade I tumor.



(a) Intra-Tumor Structure (b) MRI scan with Edema and tumor

Figure 1: Brain Tumors and Edema in MRI scan

- Grade III : The malignant tissue has cells that look very different from normal cells. The abnormal cells are actively growing.

- Grade IV : The malignant tissue has cells that look most abnormal and tend to grow quickly.

A large variety of imaging modalities are used for mapping tumor but MRI is preferred over all other modalities because of non invasive and good soft tissue contrast. In MRI there is no need to expose patient to high ionizing radiations. Various types of MRI sequences used in brain imaging are as follows.

- $T1$ weighted MRI (T_{1w})- This allows easy annotation of healthy tissues.

- $T1$ weighted MRI with contrast enhancement (T_{1wc})- This makes brain tumor borders more brighter.

- $T2$ weighted MRI (T_{2w})- Edema region can be seen clearly.

- Fluid Attenuated Inversion Recovery ($FLAIR$)- This is to separate edema region from cerebrospinal fluid.

2 Literature Survey:

Ayse Demirhan et al. [2] presented a new tissue segmentation algorithm that segments brain MR images into tumor, edema, white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF). T1, T2,and FLAIR MR images of 20 subjects suffering from glial tumor are studied. An algorithm for stripping the skull is proposed. The segmentation is performed using self organizing map (SOM) that is trained with unsupervised learning algorithm and fine-tuned with learning vector quantization (LVQ). Input feature vector is constructed with the features obtained from stationary wavelet transform (SWT) coefficients. The results showed that average dice similarity indexes are 91% for WM, 87% for GM, 96% for CSF, 61% for tumor, and 77% for edema.

Yeuhao Pan et al. [3] presented brain tumor grading using multiphase MRI images and compares the results with various configurations of deep learning structure and baseline Neural Networks. The MRI images are used directly into the learning machine, with some combination operations between multiphase MRIs. Compared to other researches,which involve additional effort to design and choose feature sets, the approach proposed leverages the learning capability of deep learning machine. The grading performance is presented on the testing data measured by the sensitivity and specificity. The results show a maximum improvement of 18% on grading performance of Convolutional Neural Networks based on sensitivity and specificity compared to Neural Networks. One of the limitation of this method is that the training samples, especially low grade data , are relatively small with biased training data.

Evangelia Zacharaki et al. [4] proposed a computer-assisted classification method combining conventional MRI and perfusion MRI consisting of several steps like ROI defination,feature extraction,selection and classification.The binary SVM classification accuracy, sensitivity, and specificity, assessed by leave-one-out cross-validation on 102 brain tumors, are respectively 87%, 89%, and 79% for discrimination of metastases from gliomas, and 87%, 83% and 96% for discrimination of high grade from low grade neoplasms.Major drawback of this method is ROIs for tumor are selected manually.

Algorithm	**MRI modalities**	**Approach**	**Perform Score**	**Tumor type**
Fletcher 2001	T_1 T_2 PD	Fuzzy Clustering w/ image retrieval	Match (53-91%)	na
Kaus 2001	T_1	Template-Moderated Classification	Accuracy 95%	LG,M
Ho 2002	T_1 T_{1c}	Level set w/ region competition	Jaccard (85-93%)	G, M
Prastava 2004	T_2	Generative Model w/ outlier detection	Jaccard (59-89%)	G,M
Corso 2008	T_1 T_{1c} T_2 $FLAIR$	Weighted agression	Jaccard (62-69%)	HG
Verma 2008	T_1 T_{1c} T_2 $FLAIR$ DTI	SVM	Accuracy (34-93%)	HG
Wels 2008	T_1 T_{1c} T_2	Discriminative model w/ CRF	Jaccard 78%	G
Cobzas 2009	T_{1c} $FLAIR$	Level-set w/ CRF	Jaccard (50-75%)	G
Wang 2009	T_1	Fluid vector flow	Tanimoto (60%)	na
Menze 2010	T_1 T_{1c} T_2 $FLAIR$	Generative model w/ lesion class	Dice (40-70%)	G
Bauer 2011	T_1 T_{1c} T_2 $FLAIR$	Hierarchical SVM w/ CRF	Dice (77-84%)	G

Table 1: tumor type is defined as G—Glioma (unspecified), HG—High-Grade Glioma, LG—Low-Grade Glioma, M—meningioma; "na" indicates that no information is reported.

Bjoern Menze et al. [5] compiled twenty state of the art tumor segmentation algorithms to a set of 65 multi-contrast MR scans of low-grade and high-grade glioma

patients manually annotated by up to four raters and to 65 comparable scans generated using tumor image simulation software. Quantitative evaluations revealed considerable disagreement between the human raters in segmenting various tumor sub-regions (Dice scores in the range 74%–85%), illustrating the difficulty of this task. The BRATS image data and manual annotations continue to be publicly available through an online evaluation system as an ongoing benchmarking resource.

Pavel Dvorak et al. [5]state that most medical images feature a high similarity in the intensities of nearby pixels and a strong correlation of intensity profiles across different image modalities. Correlation between local image patches is estimated. In the same way, there is a high correlation between nearby labels in image annotation, a feature that has been used in the local structure prediction of local label patches. This local structure prediction approach is tested for 3D segmentation tasks, systematically evaluating different parameters that are relevant for the dense annotation of anatomical structures. Algorithm is tested on BRATS 2015 database. Dice score obtained by this method is 75% for core and 73% for active part of the tumor.

3 Motivation:

Currently for grading the tumor, biopsy followed by microscopic studies are required and no image processing based method is available. Examining the change caused by the spread of tumor and edema on healthy tissues is very important for treatment planning. Hence, the detection of the healthy tissues is performed simultaneously with the diseased tissues. From the literature survey it is observed that although several brain tumor segmentation techniques are available, segmentation of intra-tumor parts is still challenging.

Mannual segmentationa of brain MR images is a time consuming and tiring process that can show 14%-22% differences when performed by different experts. Our aim is to design an automatic brain tumor segmentation algorithm which will overcome all the above mentioned challenges.

4 Identified Open Research Problems:

- Develop an algorithm for Brain tumor segmentation when there is high similarity between tumor boundary and rest of the area outside the tumor.
- Image processing based tumor grading system is not available to grade the severity of brain tumor.
- For the study of intera-tumor structures, existing methods to segment edema, necrotic cell etc are not efficient.
- Develope an algorithm which will differentiate between tumor, edema and infection

5 Problem Defination:

Objective is to develope a fully automatic system for segmentation of Brain Tumors along with edema, necrotic and active cells and formulating a grading system to grade the severity of Brain Tumor also to design an algorithm to differentiate between tumor and infection.

6 Importance of study/ Society application:

International and National importance: Among various diseases, cancer has become a big threat to human beings globally. According to statistical report by Central Brain Tumor Registry of United State brain tumor is the second leading cause of death in children under age 20 and in males 20-39. India is country of 125 crore population because of which all the hospitals/ health care services are overloaded. As biopsy based tumor grading is time consuming process, this image processing based system to grade the tumor will definitely help radiologists for early diagnosis.

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